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EXAMINER	
BAUSCH, SARAE L	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/072,012	TCHERNEV ET AL.	
	Examiner	Art Unit	
	Sarae Bausch	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) *1-4,15-38,40,41 and 43-49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-14,39 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *06/02, 06/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to applicants correspondence mailed 02/20/2007. The amendment to the claims mailed has been entered 09/29/2006. The amendment to the specification mailed 11/22/2006 and 02/20/2007 has been entered.

Election/Restrictions

2. Applicant's election without traverse of group II, claims 5-14, 39, 42 and SEQ ID No. 143 in the reply filed on 09/29/2006 is acknowledged.

3. Claims 1-4, 15-38, 40-41, and 43-49 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 09/29/2006.

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

It is acknowledged that the claimed nucleic acid and amino acid sequence of SEQ ID No. 143 and 144 is found in provisional, 60/265412 on pages 169-172 filed 01/31/2001. As such if the priority is perfected, the effective filing date of the instant application would be 01/31/2001.

Specification

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see, for example, page 31, line 50). Applicant is required to delete all embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

6. The title of the invention is not descriptive of the elected invention. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 5-14, 39, 42 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The claims are directed to an isolated nucleic acid encoding a mature form of a polypeptide set forth as SEQ ID NO: 144, identified as NOV37, and variants thereof. Claims are also directed to vectors and host cells and pharmaceutical compositions comprising said nucleic acids.

On page 11, lines 30-34, the specification teaches that the NOV37 is homologous to the "Ten-M2 like family" and asserts utility "in therapeutic and diagnostic applications implicated in various pathologies or conditions". The specification variously asserts that the claimed invention can be used to detect transcripts or genomic sequences encoding the same or homologous proteins (see page 796, 2nd paragraph), designed for expression of NOV37 protein in prokaryotic or eukaryotic cells (page 829, 1st full paragraph), designed for transgenic animals (see page 832, last paragraph), to make a pharmaceutical composition (page 835-838), can be applied as a therapeutic in gene therapy applications (page 801), can be used to develop various pharmaceuticals (page 825), can be used in chromosome mapping (page 845), can be used in screening assays, to identify individuals from a minute biological sample (page 839), tissue typing (page 847) and can be used in predictive medicine to diagnose and treat a wide variety of conditions (page 848). The specification asserts that NOV37 is predicted to be expressed in at least several different tissue types (see page 324, lines 1-8); however none of these teachings are specific to the claimed invention. The specification asserts that the compositions of the present invention (Nov37) will have efficacy for treatment of patients suffering from numerous disorders and disease (see page 332, last paragraph cont'd to page 333 1st paragraph). The specification asserts that the nucleic acids are useful in generation of antibodies for use in therapeutic or diagnostic methods (see page 333, lines 8-17). However, none of the teachings with regard to the asserted utilities are specific to the claimed invention. Instead, they are generic recitations of what essentially any nucleic acid might be used for, or are based on unsubstantiated properties of the nucleic acid. The specification provides no description of the uniquely useful properties of a transgenic animal made with the claimed invention, discloses no specific population of

individuals that can be identified using the claimed invention and provides no specific teaching as to which diseases within the broadly divergent set of conditions contemplated might actually be diagnosed or treated using the invention or reagents developed therewith. Thus, the asserted utilities are not specific.

The seminal decision interpreting the utility requirement of § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). At issue in Brenner was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

These utilities are not specific for the claimed set of nucleic acids because they are utilities that could be ascribed to any set of nucleic acid.

Further, these utilities are not substantial with regard to the claimed invention because it would take further experimentation in order to reasonably confirm a real world use for the asserted utilities. For example, a nucleic acid may be utilized to obtain a protein. The protein could then be used in conducting research to functionally characterize the protein. The need for such research clearly indicates that the protein and/or its function is not disclosed as to a currently available or substantial utility. A starting material that can only be used to produce a final product does not have substantial asserted utility in those instances where the final product

is not supported by a specific and substantial utility. In this case, none of the proteins that are to be produced as final products resulting from processes involving claimed nucleic acids have specific and substantial utilities. The research contemplated by applicant(s) to characterize potential protein products, especially their biological activities, does not constitute a specific and substantial utility. Identifying and studying the properties of a protein itself or the mechanisms in which the protein is involved does not define a "real world" context or use. Similarly, the other listed and asserted utilities as summarized above or in the instant specification are neither substantial nor specific due to being generic in nature and applicable to a myriad of such compounds. Neither the specification as filed nor any art of record discloses or suggests any property or activity for the nucleic acid and/or protein compound(s) such that another non-asserted utility would be well established for the compounds.

The instant invention is an invitation to one of skill in the art to undertake further research and experimentation to determine whether in fact the claimed array has a real world utility.

In the decision Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966), the Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

> [it] is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.[1]

Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

The asserted generic utilities for the claimed nucleic acid— diagnostic and therapeutics of multiple disorders —does not satisfy the utility requirement of § 101. Such a use does not provide a specific benefit in currently available form.

It is not questioned that the claimed nucleic acid could be used for the recited utilities. However, the specification provides no guidance to allow a skilled artisan to use the nucleic acids in any practical way. The specification simply provides no guidance regarding what the information derived from using the nucleic acid would mean. Assume, for example, that a nucleic acid of SEQ ID No. 144 was expressed in thyroid and the researcher observed that the

[1] The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would

expression of the gene the nucleic acid was a portion of was increased when a cell was treated with a particular agent. The specification provides no basis on which a skilled worker would be able to determine whether that result is meaningful. Maybe the meaning in a change in expression would depend on other factors, but again the specification provides no hint what other factors might be important. Would it depend on what agent is used, what probe is used, the behavior of other genes (if so, which genes and what behavior is significant), the degree of increase? The specification simply provides no guidance as to how to interpret the results that might be seen using the claimed nucleic acid sequence in a hybridization-based gene expression assay.

In effect, the position is that the claimed nucleic acid are useful because those of skill in the art could experiment with them and figure out for themselves what any observed experimental results might mean. Such a disclosure does not provide a "specific benefit in currently available form." Rather, the instant case seems analogous to Brenner. In Brenner, the applicant claimed a method of making a compound but disclosed no utility for the compound. 383 U.S. at 529, 148 USPQ at 693. The Court held that a process lacks utility if it produces a product that lacks utility. Id. at 534, 148 USPQ at 695. Here, the applicants claim a product asserted to be useful in a method of generating gene-expression data, but the specification does not disclose how to interpret those data. Just as the process claimed in Brenner lacked utility because the specification did not disclose how to use the end-product, the product claims here lack utility, because the specification does not disclose how to use the nucleic acid sequence.

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apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

The Supreme Court noted that the patent system contemplates a basic quid pro quo: in exchange for the legal right to exclude others from his invention for a period of time, an inventor discloses his invention to the public. See Brenner, 383 U.S. at 534, 148 USPQ at 695. The Brenner Court held that the grant of patent rights to an applicant is justified only by disclosure of an invention with substantial utility – a specific benefit in currently available form. Until the invention has been refined and developed to this point, the Court held, the applicant has not met his side of the bargain, and has not provided a disclosure sufficient to justify a grant of the right to exclude others. See id. While a specification need not disclose what is well known in the art, that rule does not excuse an applicant from providing a complete disclosure. See Genentech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997): "It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement."

Thus, the burden would be on the artisan using the nucleic acid sequence to determine a real world utility for the nucleic acid that is specific and substantial, and the claims are so rejected for lacking a specific and substantial utility.

9. Claims 5-14, 39, and 42 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly.

Claim Rejections - 35 USC § 112- Second Paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 5-7, 10-14, 39 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5, parts (e) and (f) are indefinite. The claims read as follows:

"An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence selected from...(e) a nucleic acid fragment encoding at least a portion of a polypeptide...", and, "An isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide comprising an amino acid sequence selected from...(f) a nucleic acid molecule comprising a complement of (a), (b), (c), (d) or (e)."

The claims read as though the nucleic acid molecule encodes a polypeptide comprising an amino acid sequence that is a nucleic acid. Furthermore, a nucleic acid molecule encoding a complement of a nucleic acid encoding a given polypeptide would not itself encode a polypeptide as recited in the preamble. The metes and bounds of the claimed subject matter are unclear because they appear to be inconsistent with the properties of polypeptides and nucleic acids.

Claim 5, part (e) is also indefinite in limiting the nucleic acid to being a fragment without indicating the relative whole. A fragment is generally understood to be a part broken off or detached from a whole. The meaning of the term is therefore unclear unless the "whole" is identified. In other words, it is unclear what distinguishes the nucleic acid fragment of claim 5(e) from any other nucleic acid encoding at least a portion of a polypeptide comprising SEQ ID NO: 52, especially in light of the fact that a fragment encoding the entirety of SEQ ID NO: 52 is still within the scope of the claim.

Claims 6-14, 39 and 42 are indefinite insofar as they depend from claim 5.

Claim Rejections - 35 USC § 112-Description

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 5-14, 39 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

In the instant case, claims are directed to a nucleic aid encoding variants of the polypeptide sequence set forth as SEQ ID NO: 144, wherein a variant is a polypeptide whose residues may be changed from the disclosed sequence while still encoding a protein that maintains its Ten-M2-like activities and physiological functions, or a functional fragment thereof (*Id.*). In claims 6 and 7, the variant is limited to being a naturally occurring allelic nucleic acid

variant or a naturally occurring polypeptide variant. Thus, the variant of the claims is generic to a structurally divergent set of nucleic acid molecules encoding any polypeptide having up to about 60% of the amino acids changed relative to the disclosed amino acid sequence, or fragment thereof, and retaining some unspecified ten M2 protein -like activity.

The Guidelines for Written Description state: "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus" (Federal Register, Vol. 66, No. 4, Column 3, page 1106). "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus" (MPEP §2163(3)(a)(ii)).

In the instant case, although several naturally occurring sequence variants of the claimed invention are disclosed in the application (*i.e.*, nucleic acids encoding SEQ ID NO: 478-489) the specification fails to disclose which of the sequence variants actually have tem-m2 protein -like activities and physiological function, which activities and functions are not specifically disclosed in the application (*Id.*). Thus, it is not clear how many of the disclosed species are actually representative of the claimed genus of "variants". Furthermore, as stated in MPEP 2163(I)(A), "A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by

a method of obtaining the claimed sequence." In the instant case, the disclosure provides only a vague unsubstantiated assertion as to the function of the claimed nucleic acid and no disclosure at all of important structural determinants for the ten-M2 protein -like activities and physiological functions. Thus, the skilled artisan could not possibly envision the structural determinants of ten M2 protein -like activities and physiological functions such that one would acknowledge Applicant was in possession of the claimed variants at the time of filing.

With regard to naturally occurring allelic variants, the disclosure provides no written description for any naturally occurring variants of NOVX beyond those explicitly disclosed in the application. The general knowledge in the art concerning alleles does not provide any indication of how the structure of one allele is representative of unknown alleles. The nature of alleles is that they are variant structures, and in the present state of the art the structure of one does not provide guidance to the structure of others.

The claims are drawn to an isolated nucleic acid comprising an amino acid sequence of a mature form of he amino acid sequence of SEQ ID No. 144, a variant of the mature form of SEQ ID No. 144, a nucleic acid fragment encoding at least a portion of a polypeptide comprising the amino acid of SEQ ID No. 144. The claims are further drawn to a nucleic acid comprising an isolated nucleic acid that hybridizes to a nucleic acid sequence of SEQ ID No. 143. The recitation of "an" amino acid broadly encompasses variants, homologs, and mutants with a minimum of two amino acids of SEQ ID No 144 from any source. While the specification teaches SEQ ID 144 and the nucleic acid sequence of SEQ ID No. 143, the recitation of "variant" broadly encompasses variants, mutants and homologs of SEQ ID NO 143 and 144, from any source. The recitation of the complement of a fragment of SEQ ID NO 24 broadly

encompasses variants, mutants and homologs of SEQ ID NO. 24 that are not described in the specification. The recitation of "hybridization" language allows for polynucleotides with substantial variation with regard to SEQ ID NO 143 and thus broadly encompasses variants, mutants, and homologs of SEQ ID NO 143, from any source.

While the specification teaches SEQ ID NO 143-144, the specification provides insufficient written description to support the broad genus encompassed by the claims. The instant claims are drawn to undisclosed sequences encoding modification that have not been contemplated. The specification provides insufficient written description to support the genus encompassed by the claim. Absent a written description, the specification fails to show that the applicant was "in possession of the claimed invention" at the time the application for the patent was filed. Further, the genus of polynucleotides comprised by the claim is a large variable genus and also reads on undisclosed genomic sequences. The specification only discloses a selected number of species of the genus; i.e. SEQ ID NO 143-144, which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the genus, which include full length genes, mutants, variants, and homologs of ten-M2 like protein from any source. One of skill in the art would conclude that Applicant was not in possession of the claimed genus because a description of any given member of the genus, or even multiple species within the genus, provides no support for the structure of any species within the genus that is not disclosed. Thus one skilled in the art cannot reasonably conclude that applicant had possession of the claimed genomic sequences, as well as mutants, variants, and homologs from any source at the time the instant application was filed with respect to claims 15-14, 39 and 42.

Claim Rejections - 35 USC § 112-Enablement

14. Claims 5-14, 39 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

First, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Furthermore, even if Applicant could identify a specific and substantial asserted utility, using the claimed invention for any of the purposes set forth in the specification would require undue experimentation.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

Nature of the invention and Breadth of the claims

The claims are directed to an isolated nucleic acid encoding a mature form of a polypeptide set forth as SEQ ID NO: 144, identified as NOV37, and variants thereof. Claims are

also directed to vectors and host cells and pharmaceutical compositions comprising said nucleic acids. As discussed above, the claims broadly encompass nucleic acids encoding polypeptides of substantial structural diversity. The claims are further drawn to pharmaceutical compositions comprising an isolated nucleic acid of SEQ ID No. 143. Thus the claims encompass nucleic acid that encode a polypeptide that is biological active or antigenic and encompass composition for therapeutic purposes. The claims encompass pharmaceutical compositions for treatment of any disease, infection or cancer. The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims.

State of the prior art and level of predictability in the art

As described above, the closest art discloses a nucleic acid encoding a polypeptide that is approximately 95% identical to the instant SEQ ID NO: 144. However, the art fails to teach any specific and substantial useful property for the nucleic acid disclosed therein. In fact, the art teaches that the function of the related protein is unknown (Oohashi et al, JCB, 1999, pp.575-576). Thus, the art does not suggest any particular useful property shared by any protein having 85% identity with the protein disclosed therein or nucleic acid encoding the protein. Furthermore, art does not suggest any therapeutic or diagnostic utility for an ten M2 protein, let alone a nucleic acid encoding a protein having limited structural similarity to ten M2. Thus, the skilled artisan is fully dependent upon the teachings of the instant application to provide a written description of the manner and process of using the invention in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, use the same without undue experimentation.

An analysis of the prior art as of the effective filing date of the present application shows

the complete lack of documented success for any treatment based on gene therapy. In a review on the current status of gene therapy, both Verma et al (Nature, Vol. 389, pages 239-242, 1997; e.g. page 239, paragraph 1) and Palù et al (J. Biotechnol. Vol. 68, pages 1-13, 1999; e.g. Abstract) state that despite hundreds of clinical trials underway, no successful outcome has been achieved. The continued, major obstacles to successful gene therapy are gene delivery and sustained expression of the gene. Regarding non-viral methods for gene delivery, Verma et al indicate that most approaches suffer from poor efficiency and transient expression of the gene (e.g. page 239, right column, paragraph 2). Likewise, Luo et al (Nature Biotechnology, Vol. 18, pages 33-37, 2000) indicate that non-viral synthetic delivery systems are very inefficient (e.g. Abstract; page 33, left column, paragraphs 1 and 2).

The area of the invention is unpredictable. As discussed above, the method of *in vivo* gene therapy is highly complex and unpredictable. Indeed, recent gene therapy protocols have demonstrated unpredictable outcomes resulting from an unexpected inflammatory reaction to an adenoviral vector in a patient and the insertional mutagenesis of a gene resulting in a leukemia-like condition in children being treated for severe combined immunodeficiency (Edelstein et al, J. Gene Med. Vol. 6, pages 597-602, 2004; e.g. page 599, The hopes and the setbacks). The skilled artisan at the time the present invention was made recognized the difficulty of achieving sufficient heterologous gene expression to induce any therapeutic effect.

Amount of direction provided by the inventor and existence of working examples

As described above, the specification variously teaches that the claimed invention can be used to make a transgenic animal, to make a pharmaceutical composition, can be applied as a

therapeutic in gene therapy applications, can be used to develop various pharmaceuticals and can be used in predictive medicine to diagnose and treat a wide variety of conditions. However, the specification fails to provide information fundamental to practicing any of the asserted utilities. Although, the specification provides detailed instruction regarding how to make a transgenic animal, which is routine in the art, there is no guidance as to the useful properties of the transgenic animal. Thus, the skilled artisan must resort to experimentation to discover how to use the transgenic animal. The specification provides detailed guidance regarding how one might make and administer a pharmaceutical composition comprising the claimed invention or a pharmaceutical identified using the claimed invention. However, the specification omits critical teachings such as which pharmaceutical composition (*i.e.*, nucleic acid, antibody, agonist or antagonist) should be administered, which patient population should be treated and an effective dosage and route of administration. Each of these parameters would have to be established experimentally before any pharmaceutical composition comprising the invention or identified using the invention could be used. Likewise, any diagnostic utility for the claimed invention would have to be established experimentally because the specification fails to teach what, if any, condition could be diagnosed using the invention or diagnostics developed using the claimed invention, and fails to teach what indicators (*i.e.*, increased expression, decreased expression, point mutation, *etc.*) are diagnostic of any condition. Thus, even if a specific and substantial utility can be found in the specification, the disclosure fails to provide a written description of the manner and process of using the invention in such full, clear, concise, and exact terms as to enable the skilled artisan to use the same without undue experimentation.

Relative skill of those in the art and quantity of experimentation needed to make or use the invention:

Although the relative level of skill in the art is high, the skilled artisan would not be able to apply the instant invention in a specific "real world" utility without first engaging in undue experimentation. As described above, the art fails to teach any functional properties or any specific or substantial utility for Ten M2 protein, and the instant specification provides only broad outlines of potential uses for the claimed invention. Given no more than what is available in the art, the skilled artisan would have to engage in undue empirical experimentation to reasonably establish a substantial research, diagnostic or therapeutic use for the claimed invention or any agent identified using the claimed invention. Therefore, the disclosure fails to enable the claimed subject matter.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. Claims 5-14, 39 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Oohashi et al (JCB, 1999, vol 145, pp.563-577).

Oohashi et al. teach a nucleic acid sequence comprising a variant of the mature form the amino acid sequence of SEQ ID No. 144 (see figure 1, ten-m2 protein) (claim 5). Oohashi et al teach the nucleic acid molecule comprises a naturally occurring allelic nucleic acid variant,

encoding a polypeptide comprising the amino acid sequence of the naturally occurring variant. (claim 6-7) and differs by a single nucleotide of SEQ ID No. 143 (claim 8) (see alignment provided and figure 1). With regard to claim 9-11, Oohashi et al. teach a nucleic acid sequence comprising a coding sequence differing by one or more nucleotide sequences from a coding sequence encoded by SEQ ID No. 144 (see figure 1).

With regard to claims 12-14, 39, and 42, Oohashi et al. teach a cell comprising the nucleic acid comprising a variant of the mature form of the amino acid sequence of SEQ ID No. 144 (see figure 1 and isolation of cDNA of ten-m2, page 564 and protein purification, page 565).

Conclusion

17. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

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